

In Vitro Activities of Lomefloxacin and Temafloxacin against Pathogens Causing Diarrhea

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The in vitro activities of temafloxacin (A63004) and lomefloxacin (SC-47111; NY-198) were compared with those of seven other antibiotics against 146 isolates of bacterial enteric pathogens, including *Campylobacter jejuni* and *Campylobacter coli*. Ciprofloxacin was the most active drug against the *Salmonella*, *Shigella*, *Yersinia*, and *Vibrio* spp. tested. Lomefloxacin, temafloxacin, and difloxacin were the most active drugs tested against *Campylobacter* spp. (MIC for 90% of strains, 0.125 to 0.25 µg/ml).

A number of fluoroquinolones have been shown to have good activities against common bacterial enteric pathogens (6-8). Both lomefloxacin (SC-47111; NY-198) and temafloxacin (A63004) have been shown to have activities against *Salmonella*, *Shigella*, and *Yersinia* spp. comparable to those of older quinolones (1, 2, 9, 11, 20). However, there are few data on the in vitro activities of these new quinolones against *Campylobacter jejuni*, *Campylobacter coli*, *Clostridium difficile*, and *Vibrio* spp. We therefore evaluated the activities of these two new quinolones against 146 enteric pathogens and compared their activities with those of four other quinolones and three other antimicrobial agents.

Susceptibility testing was performed with Mueller-Hinton agar and standard agar dilution methods except with *C. jejuni*, *C. coli*, and *Clostridium difficile*, for which Wilkins-Chalgren agar was used (6). Organisms were prepared by transferring three to five colonies from an overnight culture of the organism into tryptic soy broth. After 4 h of growth, turbidity was adjusted with sterile saline to a 0.5 McFarland standard. For *Clostridium difficile*, *C. jejuni*, and *C. coli*, three to five colonies from a 24-h growth were inoculated in Wilkins-Chalgren broth, adjusted to a 0.5 McFarland standard, and inoculated onto agar. Incubation temperature was 35°C for all organisms except *C. jejuni* and *C. coli*, which were incubated at 42°C. Plates were inoculated with a multipoint replicator (Cathra, St. Paul, Minn.) assigned to deliver exactly 0.001 ml per spot to the surface of antibiotic-containing agar. Inocula contained approximately 10⁴ CFU of organisms per spot. Plates were inoculated from the lowest to the highest concentration of antibiotic. All organisms except *Clostridium difficile*, *C. jejuni*, and *C. coli* were incubated in ambient air. *Clostridium difficile* plates were incubated in an anaerobic glove box. *C. jejuni* and *C. coli* plates were placed in a microaerobic atmosphere by using the polybag technique (6). These plates were read at 24 and 48 h. Control plates without antibiotics were inoculated before and after each antibiotic series. Appropriate control organisms were included on all plates. MICs were defined as the lowest concentrations of antibiotic that allowed no visible growth.

A total of 146 isolates were tested. Except for *C. coli*, all isolates were of human origin and taken from our clinical microbiology laboratory at Rush-Presbyterian-St. Luke's

Medical Center. Hippurate hydrolysis was done as previously described (10). All *C. jejuni* cells were hippurate positive, and all *C. coli* cells were hippurate negative. Organisms were stored at -70°C and were subcultured at least twice on appropriate media before susceptibility testing.

Compounds used in the study were obtained as follows: ciprofloxacin from Miles Pharmaceuticals, West Haven, Conn.; norfloxacin from Merck Sharp & Dohme, Rahway, N.J.; temafloxacin, difloxacin, and erythromycin from Abbott Laboratories, North Chicago, Ill.; lomefloxacin from Searle Pharmaceuticals, Skokie, Ill.; nalidixic acid from Aldrich Chemical Co., Milwaukee, Wis.; and trimethoprim-sulfamethoxazole and doxycycline from Sigma Chemical Co., St. Louis, Mo.

Thymidine phosphorylase (0.1 U/ml; Sigma) was added to plates when trimethoprim-sulfamethoxazole was tested.

Table 1 shows the comparative activities of temafloxacin and lomefloxacin against bacterial pathogens, expressed as the MICs for 50 and 90% of the strains and the range. Overall, ciprofloxacin was the most active drug tested against *Salmonella*, *Shigella*, *Vibrio*, and *Yersinia* spp. Temafloxacin, difloxacin, and lomefloxacin showed activities against *C. jejuni* comparable to that of ciprofloxacin. All of the quinolones tested, with the exception of norfloxacin, were more active than erythromycin against this organism. Temafloxacin was the most active agent tested against *C. coli*. Of the quinolones tested, temafloxacin had the greatest activity against *Clostridium difficile*, requiring MICs of from 2 to 4 µg/ml. Ciprofloxacin and difloxacin were slightly less active, with MICs for 90% of the strains of 8 µg/ml, which is in agreement with results from previous studies (3, 4). Lomefloxacin and norfloxacin were the least active of the quinolones against *Clostridium difficile*, with MICs for 90% of the strains of 64 µg/ml. The reason for this range of MICs with *Clostridium difficile* is unclear. Van der Auwera et al. (19) report somewhat higher MICs of lomefloxacin for *C. jejuni*. This may be related to geographical variation but is more likely due to methodologic differences.

Ciprofloxacin and norfloxacin have proven effective in the prophylaxis of traveler's diarrhea, the therapy of traveler's diarrhea, the treatment of acute diarrhea in adult nontravelers, and the treatment of typhoid fever and chronic *Salmonella* carriage (5, 12-14, 16, 18). Given the good in vitro activities of lomefloxacin and temafloxacin against the en-

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TABLE 1. Comparative activity of six quinolone antimicrobial agents and three other antimicrobial agents against bacterial enteropathogens

Organism	No. of isolates	Antimicrobial agent	MIC ($\mu\text{g/ml}$) ^a		
			Range	50%	90%
<i>Salmonella</i> spp.	28	Temafloracin	0.015–0.5	0.06	0.125
		Lomefloxacin	0.03–2.0	0.125	0.50
		Difloxacin	0.125–1.0	0.125	0.25
		Nalidixic acid	4.0–16.0	4.0	16.0
		Norfloxacin	0.06–1.0	0.125	0.25
		Ciprofloxacin	≤ 0.008 –0.015	≤ 0.008	≤ 0.008
		Trimethoprim-sulfamethoxazole	0.06–0.5	0.125	0.5
		Doxycycline	1.0–32.0	4.0	16.0
<i>Shigella</i> spp.	20	Temafloracin	≤ 0.008 –0.06	0.015	0.03
		Lomefloxacin	≤ 0.008 –0.06	0.06	0.06
		Difloxacin	0.015–0.25	0.06	0.125
		Nalidixic acid	1.0–4.0	2.0	4.0
		Norfloxacin	≤ 0.008 –0.03	0.015	0.03
		Ciprofloxacin	≤ 0.008 –0.015	≤ 0.008	≤ 0.008
		Trimethoprim-sulfamethoxazole	≤ 0.03 –>64.0	0.125	0.5
		Doxycycline	0.5–32.0	4.0	16.0
<i>Campylobacter jejuni</i>	25	Erythromycin	8.0–>64.0	32.0	>64.0
		Temafloracin	0.03–0.25	0.06	0.125
		Lomefloxacin	0.03–0.25	0.06	0.125
		Difloxacin	0.125–0.25	0.25	0.25
		Nalidixic acid	2.0–8.0	4.0	8.0
		Norfloxacin	0.25–2.0	0.5	1.0
		Ciprofloxacin	0.25–0.5	0.25	0.5
		Trimethoprim-sulfamethoxazole	2.0–>32.0	16.0	32.0
<i>Campylobacter coli</i>	26	Doxycycline	0.25–16.0	1.0	8.0
		Erythromycin	0.125–2.0	0.5	1.0
		Temafloracin	0.015–0.125	0.015	0.125
		Lomefloxacin	0.125–0.5	0.25	0.25
		Difloxacin	0.015–0.5	0.125	0.25
		Nalidixic acid	0.5–8.0	4.0	8.0
		Norfloxacin	0.25–2.0	0.5	1.0
		Ciprofloxacin	0.015–0.25	0.06	0.25
<i>Yersinia enterocolitica</i>	17	Trimethoprim-sulfamethoxazole	2.0–>32.0	8.0	>32.0
		Doxycycline	0.06–>32.0	0.25	>32.0
		Erythromycin	0.25–>32.0	2.0	>32.0
		Temafloracin	≤ 0.008 –0.25	0.015	0.06
		Lomefloxacin	0.015–0.25	0.03	0.25
		Difloxacin	0.025–0.25	0.03	0.125
		Nalidixic acid	0.5–4.0	1.0	2.0
		Norfloxacin	≤ 0.008 –0.125	0.06	0.125
<i>Vibrio</i> spp. (3 <i>V. cholerae</i> , 7 <i>V. parahaemolyticus</i>)	10	Ciprofloxacin	≤ 0.008 –0.015	≤ 0.008	0.015
		Trimethoprim-sulfamethoxazole	≤ 0.03 –0.25	0.06	0.25
		Doxycycline	0.25–32.0	1.0	2.0
		Erythromycin	16.0–>32.0	32.0	>32.0
		Temafloracin	≤ 0.008 –0.25	0.25	0.25
		Lomefloxacin	≤ 0.008 –0.25	0.125	0.125
		Difloxacin	≤ 0.008 –0.125	0.125	0.125
		Nalidixic acid	0.125–1.0	0.25	0.25
<i>Clostridium difficile</i>	20	Norfloxacin	≤ 0.008 –0.125	0.03	0.03
		Ciprofloxacin	≤ 0.008 –0.015	≤ 0.008	≤ 0.008
		Trimethoprim-sulfamethoxazole	≤ 0.03 –0.125	0.03	0.03
		Doxycycline	0.125–0.5	0.25	0.25
		Erythromycin	4.0–8.0	4.0	4.0
		Temafloracin	2.0–4.0	4.0	4.0
		Lomefloxacin	32.0–64.0	32.0	64.0
		Difloxacin	4.0–8.0	8.0	8.0
<i>Clostridium difficile</i>	20	Norfloxacin	32.0–64.0	32.0	64.0
		Ciprofloxacin	2.0–16.0	8.0	8.0
		Trimethoprim-sulfamethoxazole	1.0–8.0	2.0	4.0
		Erythromycin	≤ 0.5 –4.0	1.0	4.0

^a 50% and 90%, MIC for 50 and 90% of isolates, respectively.

teropathogens tested and given their favorable pharmacokinetics (2, 15, 17), it is expected that they too may have a place in the prophylaxis and treatment of acute bacterial gastroenteritis.

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